

In the Sequence Listing:

Applicants hereby request that the as filed sequence listing, pages 78–99, be replaced with the supplemental sequence listing submitted herein as Attachment A.

REMARKS

I. Claims Pending in The Application:

In view of the above amendments, claims 1–11 and 15–21 are now pending in this Application. In view of the following remarks and the changes hereinabove, Applicants respectfully request that the Patent Office reconsider and withdraw the various grounds for objection and rejection set forth in the Office Action. The amendments to the claims introduce no new matter.

II. Election/Restriction

At paragraph 3 of the Office Action, the Examiner has issued a restriction requirement to one of the inventions under 35 U.S.C. §121:

- | | |
|------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Group I: | Claims 1-11, 15-21, 26 and 27, drawn to Apo-2DcR polypeptide, chimeric polypeptide, nucleic acid, vector, host cell, and method of using the nucleic acid for polypeptide production, classified in class 435, subclass 69.1. |
| Group II: | Claims 12-14, 26, and 27, drawn to antibody and article of manufacture comprising the antibody, classified in class 530, subclass 387.1. |
| Group III: | Claims 22-23, drawn to transgenic animal, classified in class 800, subclass 2. |
| Group IV: | Claims 24-25, drawn to knockout animal, classified in class 800, subclass 2. |

Group V: Claims 28-29, drawn to method of modulating apoptosis, classified in class 514, subclass 12.

Applicants' Election

Applicants hereby affirm the election to prosecute the claims of Group I in the present application. The claims drawn to the non-elected inventions have been canceled without prejudice in the above-amendment.

III. Information Disclosure Statement

At paragraph 6 of the Office Action, the Examiner states that no references were found accompanying the IDS submitted December 17, 1997.

In response to this item, Applicants respectfully point out that copies of the references were included with the IDS submitted December 17, 1997 and have attached hereto a copy of a date stamped return postcard showing that the form 1449 with 244 references was received in the U.S. Patent Office on December 22, 1997 (submitted herein as Attachment B). Given the number of references which were already provided, Applicants respectfully request that a renewed search for these references in the PTO be conducted. If these references cannot be found, it would be appreciated if the Examiner could telephone the undersigned attorney and Applicants will again provide copies to the Patent Office.

Applicants wish to point out that a Supplemental Information Disclosure Statement citing three additional references is being filed herewith.

IV. Sequences

At paragraphs 7 and 8 of the Office Action, the Examiner asserts that the sequences in lines 1 and 3 of page 64 have not been assigned sequence identifiers and, therefore, fail to comply with the requirements of 37 C.F.R. 1.821 through 1.825.

In response to this item, Applicants respectfully point out that the sequence identifiers for the sequences in lines 1 and 3 of page 64 are found at page 64, lines 6 and 8 respectively. As it

was not possible to include all of the residues in this sequence comparison in a single line, the comparison continues on the next lines of this page (i.e. lines 6 and 8), which also contain the sequence identifiers for these sequences.

V. Sequences Presented in Figures

At paragraph 9 of the Office Action, the Examiner states that compliance with the requirements of 37 C.F.R. 1.821 through 1.825 requires that the sequences in Figures 1A, 1B, 2, 8 and 9 be identified with a unique sequence identifier either in the figure or its Brief Description at page 10. In addition, the Examiner states that all references to a figure with a sequence must also use the sequence identifier.

Applicants' amendments to the specification hereinabove and their submission of a substitute sequence listing are believed to bring the application into compliance with the requirements of Sections 1.821-1.825.

VI. Drawings

At paragraph 10 of the Office Action, the Examiner notes that the two sheets of drawings which are labelled "Figure 8" in the instant specification should be renumbered "Figures 8A and 8B".

On indication of allowable subject matter, the formal matters pointed out by the Examiner relating to Figure 8 will be addressed.

VII. Rejections Under 35 U.S.C. §112, Second Paragraph:

At paragraph 11 of the Office Action, the Examiner asserts that claims 1-3 are indefinite in their recitation of "about 80%" because the specification "does not describe whether this term is intended to mean, for example, 79-100% or 60-100%".

Applicants respectfully traverse the Examiner's rejection and note that in this art accepted technique for evaluating the relationship between amino acid or nucleotide sequences, the skilled

artisan understands the use and meaning of such identity values. The case law supports Applicants use of the term "about". See e.g. Orthokinetics Inc. v. Safety Travel Chairs Inc., 1 USPQ 2d 1081, 1088 (Fed. Cir. 1986). In particular, courts note that the use of the descriptive term "about" when necessary to explain ranges in a patent, "does not render a claim indefinite under 35 U.S.C. 112, . . . 'About is not broad or arbitrary but rather is a flexible term with a meaning similar to 'approximately'. See e.g. Syntex (U.S.A.) Inc. v. Paragon Optical Inc., 7 USPQ 2d 1001, 1038 (D. Ariz. 1987). For these reasons, Applicants respectfully request the withdrawal of this rejection.

The Examiner also asserts that claims 1-3 are indefinite because it is unclear what is encompassed by the claims because the specification does not define how "identity" is to be calculated and the art has not recognized one way of calculating identity. Applicants respectfully traverse the Examiner's rejection and point out that at page 13, lines 9-23 the specification defines identity, specifically teaching that

"Percent (%) amino acid sequence identity" with respect to the Apo-2DcR sequences identified herein is defined as the percentage of amino acid residues in a candidate sequence that are identical with the amino acid residues in the Apo-2DcR sequence, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity, and not considering any conservative substitutions as part of the sequence identity. Alignment for purposes of determining percent amino acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software such as ALIGN or Megalign (DNASTAR) software. Those skilled in the art can determine appropriate parameters for measuring alignment, including any algorithms needed to achieve maximal alignment over the full length of the sequences being compared.

This definition of "Percent (%) amino acid sequence identity" as provided in the specification readily allows the skilled artisan to identify what is encompassed by the claims. In particular, the disclosure teaches that this value is defined as the percentage of amino acid residues in a candidate sequence that are identical with the amino acid residues in the Apo-2DcR sequence. In addition, the specification teaches that this value is obtained after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity. As this definition teaches the skilled practitioner which variables to utilize in the calculation of

percent (%) amino acid sequence identity, the skilled practitioner can in fact determine what is encompassed by the claims. For these reasons, Applicants respectfully request the withdrawal of this rejection.

At paragraph 11 of the Office Action, the Examiner asserts that claims 1, 4-7, and 16-17 are indefinite because the significance of the parentheses around the SEQ ID NOs is not clear. Applicants have amended the subject claims by eliminating the reference to the Figures in order to clarify this language. Accordingly, Applicants respectfully request the withdrawal of this rejection.

The Examiner further asserts that claim 19 is indefinite and that it is unclear what the "control sequences" control. Applicants respectfully traverse the rejection and note that the specification at page 14, lines 29-31 teaches that the term "control sequences" refers to DNA sequences necessary for the expression of an operably linked coding sequence in a particular host organism. For this reason, Applicants respectfully request the withdrawal of this rejection.

In addition, the Examiner asserts that claim 21 is indefinite and that there are insufficient method steps to practice the claimed invention. Applicants have amended the claims by adding clarifying language to show that the host cell is cultured under conditions such that the Apo-2DcR polypeptide is produced. Applicants respectfully request the withdrawal of this rejection.

Lastly, it is pointed out that the cancellation of claims 26 and 27 without prejudice renders the Examiner's Section 112, second paragraph rejections of those claims moot.

VIII. Claim Objections:

At paragraph 12 of the Office Action, the Examiner objects to claims 26 and 27 as including a non-elected invention. Applicants' cancellation of claims 26 and 27, as shown in the above amendment, renders the Examiner's objections to those claims moot.

IX. Conclusion:

In light of the forgoing remarks, Applicants assert the pending claims are in condition for allowance. Notice of such allowance is solicited.

The Examiner is invited to telephone the undersigned attorney for clarification of any of the remarks above, or to otherwise further the prosecution of this case.

No fee, other than the three-month extension of time fee is deemed necessary in connection with the filing of this Amendment. If any additional extension of time fee is deemed necessary in connection with the filing of this Amendment, the Patent Office is authorized to charge the fee(s) to Deposit Account No. 13-2724.

Respectfully submitted,

Date: 2/4/99

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